

Food and Drug Administration Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Robert Niecestro, Ph.D.
Regulatory Consultant
AOI Pharmaceuticals, Inc./Keryx Biopharmaceuticals, Inc.
750 Lexington Avenue, 20th floor
New York, NY 10022

RE: (b) (4)

KRX-0401 (perifosine) MACMIS # 19525

Dear Dr. Niecestro:

As part of its monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed the AOI Pharmaceuticals, Inc./Keryx Biopharmaceuticals, Inc. (Keryx) company website¹ (www.keryx.com) (website). The website makes promotional statements about the investigational product perifosine (KRX-0401) that suggest that the drug is safe and/or effective for the purposes for which it is being investigated. As a result, the website violates the Federal Food, Drug, and Cosmetic Act (the Act) and FDA implementing regulations. 21 CFR 312.7(a).

Background

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According to the Keryx website, KRX-0401 is being investigated to treat multiple forms of cancer and for its potential to inhibit various cellular signaling pathways, including the PI3-kinase/Akt and JNK pathways.

Promotion of an Investigational Drug

Promotion of an investigational new drug is prohibited under FDA regulations at 21 CFR 312.7(a), which states that "A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or

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¹ AOI Pharmaceuticals, Inc./Keryx Biopharmaceuticals website. Available at http://www.keryx.com/page.cfm?hmid=&smid=&pg=main. Last accessed on June 30, 2011.

lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution."

The Keryx website makes numerous statements that promote KRX-0401 as safe and/or effective for the purposes for which it is being investigated or otherwise promote the drug. For example, the *About Us* and *Product Pipeline* sections of the Keryx website include statements such as the following:

- KRX-0401 has demonstrated both safety and clinical efficacy in several tumor types, both as a single agent and in combination with novel therapies.
- Its safety profile is distinctly different from that of most cytotoxic agents. KRX-0401 does not appear to cause flu-like symptoms, thrombocytopenia (decrease in platelets that may result in bleeding) or alopecia (hair loss); all of these toxicities occur frequently with many of the currently available treatments for cancer. The main side effects of KRX-0401 are nausea, vomiting, diarrhea and fatigue, but these are generally well-managed particularly at lower daily doses (50 mg or 100 mg) that have induced tumor regression.
- These trials demonstrated that KRX-0401 can be safely given to humans with a manageable toxicity profile.
- KRX-0401 has generally been well tolerated when used as a low daily dose (50 mg or 100 mg) in combination with these approved agents.

These claims suggest that KRX-0401 is safe and/or effective for the treatment of various kinds of tumors, both as a single agent and in combination with other therapies, when it has not been approved for these uses. Additionally, the totality of the above-referenced claims makes the conclusions that the drug is well-tolerated, can be safely given to humans with a manageable toxicity profile, and has a safety profile that is "distinctly different from that of most cytotoxic agents."

Since KRX-0401 is an investigational new drug, the product's indication(s), warnings, precautions, adverse reactions, and dosage and administration, have not been established and are unknown at this time. Keryx's promotion of KRX-0401 as safe and effective for purposes for which it is under investigation, by making representations such as those noted above, is in violation of 21 CFR 312.7(a). We note that the website includes the disclaimer that states, "This investigational drug product has not been approved by the US Food and Drug Administration for safety and effectiveness. This investigational drug product is still undergoing clinical study to verify its safety and effectiveness." However, this disclaimer is not sufficient to mitigate the overwhelming misleading impression conveyed by claims on Keryx's website, such as those noted above, that KRX-0401 is safe and effective.

Conclusion and Requested Action

For the reasons discussed above, the website violates the Act and FDA implementing regulations. 21 CFR 312.7(a). These statements are concerning from a public health perspective because they make promotional claims about the safety and efficacy of an investigational new drug that has not been approved by the FDA.

DDMAC requests that Keryx immediately cease the dissemination of violative promotional materials for KRX-0401 such as those described above. Please submit a written response to this letter on or before July 15, 2011, stating whether you intend to comply with this request and explaining your plan for discontinuing use of such violative materials. Please direct your response to me at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD 20705-1266, facsimile at 301-847-8444. In all future correspondence regarding this matter, please refer to MACMIS# 19525 in addition to the We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your materials for KRX-0401 comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Nisha Patel, Pharm.D. Regulatory Review Officer Division of Drug Marketing, Advertising, and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.
/s/
NISHA J PATEL 06/30/2011